Interobserver variability in MRI assessment of the severity of placenta accreta spectrum disorders

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ABSTRACT

Objective: To evaluate the level of agreement in the prenatal magnetic resonance imaging (MRI) assessment of the severity of placenta accreta spectrum (PAS) disorders in centers with high expertise in their diagnosis and management.

Methods: The MRI scans of women at risk of PAS were retrieved from the hospital electronic database and assessed by four different experts who were blinded to the final diagnosis. Each examiner was asked to judge the MRI scans according to the presence, depth and topography of placental invasion. The depth of invasion was defined as the degree of adhesion and invasion of the placenta through the myometrium and uterine serosa at the histopathological examination of the removed uterus (accreta, increta and percreta), while topography as the site of placental invasion within the uterus. The degree of inter-rater agreement (IRA) in calculating both the percentage of observed agreement among raters and the Fleiss kappa were used to analyze the data.

Results: Forty-six women were included in the study. There was an excellent agreement among the four different examiners in the assessment of the overall presence of PAS disorders (IRA: 92.1, 95% CI 86.8-94.0; K: 0.90, 95% CI 0.89-1). However, there was significant heterogeneity in the agreement among the different examiners when assessing the different MRI signs suggestive of PAS. There was also an excellent agreement in the identification of the depth (IRA: 98.9, 95% CI 96.8-100; K: 0.95, 95% CI 0.89-1.0) of PAS disorders. Conversely, the agreement in assessing the topography of placental invasion was only moderate (IRA: 72.8, 95% CI 72.7-72.9; K: 0.56, 95% CI 0.54-0.66). More importantly, when assessing parametrial invasion, which is one of the most significant prognostic factors in women affected by PAS, the agreement was moderate in judging the presence of invasion on coronal (IRA: 86.6%. 95% CI 86.5-86.7, K-: 0.69, 95% CI 0.59-0.71) and axial (IRA: 78.6, 95% CI 78.5-78.7, K: 0.56, 95% CI 0.33-0.60) planes. Likewise, the agreement in judging the presence and the number of newly formed vessels in the parametrial tissue was moderate (IRA: 88.0, 95% CI 88.0-88.1, K: 0.59, 95% CI 0.45-0.68) and weak (IRA: 66.7, 95% CI 66.6-66.7, K: 0.22, 95% CI 0.12-0.37), respectively.

Conclusion: MRI has excellent inter-observer variability in detecting the presence and depth of placental invasion, while the agreement in describing the topography of invasion is less. The findings from this study highlight the need for a standardized MRI staging system of PAS disorders,

in order to facilitate objective correlation between prenatal imaging, pregnancy outcomes and surgical management.

INTRODUCTION

Placenta accreta spectrum (PAS) disorders encompasses a heterogeneous group of conditions characterized by progressive invasion of the trophoblastic tissue through the myometrium and uterine serosa[1-3]. The prenatal diagnosis of PAS has been shown to reduce the risk of severe maternal morbidities, such as massive hemorrhage and the need for blood products, by allowing a pre-planned management in centers with high expertise in surgical management of these anomalies[4].

Ultrasound is usually the primary imaging tool in assessing women at risk for PAS, such as those presenting with placenta previa and prior cesarean delivery (CD) or uterine surgery, while magnetic resonance imaging (MRI) is performed to confirm the diagnosis and delineate the depth and topography of placental invasion, which can significantly affect maternal outcome and influence the surgical approach[5-11].

Both ultrasound and MRI have been shown to have a good diagnostic accuracy in detecting PAS. However, significant heterogeneity in the diagnosis of PAS has been reported in the recently published literature. Several factors, such as maternal characteristics, operator's experience and gestational age at assessment are likely to account for such differences[6,7,9,10].

The large majority of previously published studies assessing the inter-observer variability of either ultrasound or MRI have focused on the detection rate of PAS, without investigating the potential differences in assessing the radiological signs, such as the depth and site of placental invasion[6-9]. This is fundamental as the surgical outcomes of women affected by PAS are directly related to the depth and especially topography of placental invasion[12,13]. Furthermore, cases affected by the same degree of placental invasion may show different outcomes according to the site of invasion[14].

The aim of this study was to assess the level of agreement in the MRI assessment of the severity of PAS disorders in centers with high expertise in their diagnosis and management.

METHODS

This is a secondary analysis of a prospective study including women with placenta previa and at least one prior CD or uterine surgery undergoing MRI assessment at the Department of Radiology, Arnas Civico Hospital, Palermo, Italy, which is a referral regional center for PAS disorders, between 2007 and 2017. All women had a longitudinal ultrasound assessment in the second and third trimesters, as per local guidelines in order to detect PAS. They also had MRI evaluation in the third trimester in order to confirm the presence, depth and topography of placental invasion.

MRI scans were retrieved from the hospital electronic database and assessed by four different examiners, including three radiologists (FF, GM, SG) and one surgeon (JPJ) who are considered as experts in the diagnosis and surgical management of PAS. These 4 experts were blinded to the ultrasound diagnosis, histopathological findings and clinical data.

Each examiner was asked to judge the following features (Appendix 1, Figure 1):

1. Presence of PAS disorders
2. Depth of placental invasion
3. Location of placental invasion
4. Presence of parametrial invasion
5. Presence of newly formed vessels in the parametrial tissue
6. Placental location
7. Presence and type of placenta previa (minor vs major; minor is defined as a lower edge inside the lower uterine segment or reaching the internal os; major when the placenta partially or completely covers the internal ostium of the cervix)
8. Heterogeneous placental signal intensity, defined as heterogeneity in the placental parenchyma, which is in normal conditions characterized by a homogeneous intermediate signal intensity.[15]
9. Intra-placental T2 dark bands, defined as nodular or linear areas of low signal intensity on T2-weighted images[15].
10. Areas of hemorrhagic placental infarctions (T1 Fiat sat).
11. Presence, shape and number of placental venous lakes (lacunae)
12. Uterovesical interface
13. Bladder interface vascularization

14. Outward bulging of the placenta
15. Presence of artifacts

The reference standard was the presence of PAS detected either on histopathological assessment or, in the most severe types of invasion, on surgical evaluation. For the depth of placental invasion, the reference standard was the histopathological examination of the removed uterus[16]. Placenta accreta was diagnosed when the anchoring placental villi were attached to the myometrium rather than decidua, but without completely invading it. Placenta increta was diagnosed when the chorionic villi penetrate the myometrium, while placenta percreta was diagnosed when the chorionic villi penetrate through the myometrium to the uterine serosa or adjacent organs[16]. For the assessment of the topography of placental invasion, we adopted the anatomical classification of PAS disorders proposed by Palacios-Jaraquemada et al [12]. According to such classification, the anterior placental invasion into two sectors delimited by a plane perpendicular to the supero-inferior bladder axis, and the uterine sector bordering; the upper posterior bladder wall is called S1, and the uterine sector adjacent to the lower posterior wall, S2 (Figure 2). From an anatomical perspective, S1 invasion refers to an invasion situated in the uterine body while S2 is mainly located in the lower uterine segment or below it. The reference standard was the topography of invasion at surgery[12]. Finally, in women not undergoing hysterectomy, the presence of PAS was defined according to the International Federation of Gynecology and Obstetrics (FIGO) clinical grading system. Cases with no PAS were defined as those with complete placenta separation at the third stage[17].

All uterine specimens were assessed by the same research pathologist who were blinded to the prenatal imaging (ultrasound and MRI) and surgical findings. Furthermore, because different degrees of placental invasion may co-exist in the same uterus, every case was labelled according to the maximum observed depth of placental invasion.

All of the MRI examinations were performed on a 1.5T unit (Ingenia Philips Medical System 1.5-T unit) with body array coils, including axial, coronal and sagittal T2 -weighted half-Fourier single-shot turbo spin echo imaging (ssh-TSE) or T2 -weighted turbo spin-echo (T2 W-TSE) and/or T2 -weighted true fast imaging with steady-state precession sequence (balanced-FFE), and sagittal T 1 -weighted gradient-echo (GRE) in-phase and opposed-phase sequence. The parameters for ssh-TSE

images were: repetition time (TR) / echo time (TE), 3300–4000/70–80 msec; flip angles (FA), 90; field of view (FOV), 420–480 mm; slice thickness, 5–8 mm. For balanced-FFE images they were: TR/TE, 3700–5400/60–90 msec; FA, 90; FOV, 420–480 mm; slice thickness, 6–8 mm, and for T 1 W-GRE images they were: TR/TE, 200–230/2.3 (opposedphase)/4.6(in-phase) msec; FA, 80; FOV, 340–380 mm; slice thickness, 5–8 mm. No contrast material was used in any of the examinations.

Data analysis

continuous data were reported as median and inter-quartile range (IQR). For each of the 20 items of the questionnaire, we assessed the degree of inter-rater agreement (IRA) recording both the percentage of observed agreement among raters and the Fleiss kappa (k), with the respective 95% confidence intervals (CI)[18-23]. Fleiss k is an extension of Cohen's k when >2 raters are present, and it is obtained comparing the observed agreement to the amount of agreement expected by chance[18-19]. According to Landis and Koch k values were interpreted as: <0, poor agreement; 0.0-0.20, slight agreement; 0.21-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80, substantial agreement; 0.81-1.0, almost perfect agreement[21]. We also calculated a summary k coefficient for all items of the questionnaire, in order to quantify the overall agreement among raters. Sample size considerations were based upon the CIs of the inter-rater k statistic, and the computations were performed using the kapssi command in Stata[23]. According to the previously published studies, (a) an overall accuracy of MRI in the diagnosis of placenta accreta equal to 68%, and (b) an estimated k of 0.58 were assumed[6-9]. Based upon these data, and considering the presence of four raters, then 13 participants would provide a two-sided 95% CI for κ with a width of ±0.08.

RESULTS

Forty-six women were included in the study. The general characteristics of the study population are reported in Table 1. The median maternal age was 34.0 years (IQR 30.3-37.0); while parity and number of prior CD 1 (1-2) and 1 (1-2) respectively. The median gestational age at MRI was 33.8 weeks (IQR 33.1-34.0). The incidence of placenta accreta, increta and percreta in the study population was 15.2%, 17.4% and 50.0%, respectively.

There was an excellent agreement among the four different examiners in the assessment of the overall presence of PAS disorders (IRA: 92.1, 95% CI 86.8-94.0; K: 0.90, 95% CI 0.89-1). Despite this, there was significant heterogeneity in the agreement among the different examiners when assessing the different MRI signs suggestive of PAS. The agreement among the different examiners was strong for the presence (K: 0.90, 95% CI 0.89-1) of placental lacunae, while it was only moderate when assessing the lower uterovesical interface (K: 0.64, 95% CI 0.55-0.74) and the heterogeneous signal intensity within the placenta (K: 0.70, 95% CI 0.63-0.71).

The depth of placental invasion was based upon the histopathological examination of the removed uterus and classified into placenta accrete, increta and percreta. There was an excellent agreement in the identification of the depth (IRA: 98.9, 95% CI 96.8-100; K: 0.95, 95% CI 0.89-1.0) of PAS disorders. The IRA and K-values of the agreement when assessing the other MRI parameters are reported in Table 2.

Topography of placental invasion was judged according to the classification system provided by Palacios-Jaraquemada et al[15]. When assessing the site of placental invasion, there was moderate agreement among the different examiners (IRA: 72.8, 95% CI 72.7-72.9; K: 0.56, 95% CI 0.54-0.66), although lower than that observed in the identification of the presence and depth of invasion (Table 2).

More importantly, when assessing the parametrial invasion, which is one of the most significant prognostic factors, the agreement was moderate in judging the presence of invasion on coronal (IRA: 86.6%. 95% CI 86.5-86.7, K-: 0.69, 95% CI 0.59-0.71) and axial (IRA: 78.6, 95% CI 78.5-78.7, K: 0.56, 95% CI 0.33-0.60) planes. Likewise, the agreements in judging the presence and the number of newly formed vessels in the parametrial tissue were moderate (IRA: 88.0, 95% CI 88.0-88.1, K: 0.59, 95% CI 0.45-0.68) and weak (IRA: 66.7, 95% CI 66.6-66.7, K: 0.22, 95% CI 0.12-0.37, respectively).

DISCUSSION

Summary of the key study findings

The findings from this study demonstrate that, among experienced operators, MRI has an excellent inter-observer variability in identifying the presence and depth of PAS. Inter-observer variability is lower for the assessment of the topography of invasion, especially for the detection of parametrial invasion and the presence of newly formed vessels within the parametrial tissue, which can significantly affect maternal outcomes and the choice of an appropriate surgical approach.

Strengths and weaknesses

The main strengths of the present study rely on the evaluation of MRI scans by examiners with high expertise in the prenatal diagnosis of PAS. Furthermore, they were blinded to the clinical and histopathological findings. Moreover, the assessment included a multitude of MRI parameters. Relatively small number of included cases and high incidence of severe cases of PAS represent the major weaknesses of the study. Another potential limitation was the lack of assessment by less experienced radiologists, as reported in previously published studies. However, cases at high risk for PAS disorders should be referred to centers with high expertise in their diagnosis and management[24]. Finally, we did not use Gadolinium in any of the included women, thus we could not explore whether its administration would have led to an improved agreement among the different examiners.

Interpretation of the study findings and implications for clinical practice

The depth and topography of placental invasion are the main determinants in predicting the surgical outcome in women affected by PAS disorders[12,13].

The depth of invasion is commonly ascertained on histopathological assessment of the uterine specimen after hysterectomy. However, such assessment is retrospective and not always useful when planning surgery. Furthermore, different degrees of placental invasion may co-exist in the same uterus.

The identification of the area invaded by the placenta may provide useful information when planning surgery in women affected by PAS. Invasion in the lower uterine segment and posterior bladder may result in severe maternal complications even in early pregnancy. Surgical dissection in

cases of lower bladder invasion can cause serious maternal morbidity, especially due to narrow space, wide connection with anastomotic pedicles and the presence of fibrous tissue between the invaded area and the bladder, which make achieving adequate hemostasis very challenging. Likewise, parametrial invasion is associated with placental adherence to the retroperitoneal structures, including the iliac and ovarian vessels, bladder, and ureter[12]. Furthermore, the presence of newly formed vessels in the parametrial tissue may represent an additional risk factor for massive hemorrhage during surgery and may also lead to ureteral invasion. Conversely, upper posterior bladder invasion is relatively easier to manage mainly because bleeding is more controllable and surgical access is easier.

Despite its importance in predicting the outcome in PAS disorders, the assessment of the topography of placental invasion has not been consistently reported in the published literature. Accurate knowledge of the topography of placental invasion is fundamental for prenatal counselling when considering the potential surgical risks or the feasibility of conservative respective techniques such as Triple-P procedure or one-step conservative surgery[25,26]. Although the choice of the optimal surgical approach is undertaken after the visualization of the actual degree of placental invasion at the opening of the peritoneum, appropriate knowledge of the topography of invasion would enable the surgeon to consider the different management options before surgery.

Despite its importance, there is no study reporting the diagnostic accuracy of ultrasound in describing the topography of placental invasion in women with PAS, which has been reported only using prenatal MRI. One of the most objective attempts to categorize the topography of invasion has been recently provided by Palacios-Jaraquemada et al using MRI[12]. The importance of such classification system relies on its ability to predict surgical outcome, with women presenting with S2 invasion being at higher risk of severe complications in view of the higher risk of parametrial invasion.

In the present study, there was a moderate agreement in the description of the topography of placental invasion among the different examiners. Likewise, there was also a moderate agreement in assessing the presence of parametrial invasion and newly formed vessels. These findings highlight the need for future multicenter collaboration between clinical and research groups in order to develop an objective prognostic prenatal staging system .

Conclusions

MRI has an excellent inter-observer agreement in detecting the depth of placental invasion. However, the agreement in ascertaining the topography of invasion is low. This highlights the need for an objective standardization of MRI assessment of PAS disorders and the creation of a reproducible prognostic prenatal staging system.

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Figure legend

Figure 1:

1a: Normal appearance of the placenta with three layers of normal myometrium: the hypo-intense outer and the inner layers surround the more hyper-intense middle layer, which contains vessels.

1b: Placenta percreta in the S2 segment. Intra-placental dark bands and outward bulging of the placenta (arrows)

1c: Placenta creta without bladder invasion.

1d: Placenta percreta with S1 invasion.

1e: Placenta percreta with S2 invasion.

1f: Intra-placental dark bands (arrows) and bladder invasion (arrowheads)

1g: Placenta percreta with bladder invasion and newly formed vessels arrows).

1h: Dark band and heterogeneous signal within the placenta**.**

1i: Focal outward bulging of the placenta.

1l and 1m: Artifacts due to fetal movements.

Figure 2: The anterior placental invasion into two sectors delimited by a plane perpendicular to the supero-inferior bladder axis, and the uterine sector bordering; the upper posterior bladder wall is called S1, and the uterine sector adjacent to the lower posterior wall, S2

Table 1. General characteristics of the study population.

Characteristic	
Maternal age in years*	34.0 (30.3-37.0)
Parity*	1 (1-2)
Prior CD*	1 (1-2)
Gestational age at MRI*	33.8 (33.1-34.0)
Position of the placenta Anterior Posterior Lateral	 100 (46/46) 0 (0/46) 0 (0/46)
Final diagnosis • Placenta previa (no PAS) • Placenta creta (%) • Placenta increta (%) • Placenta percreta (%)	 17.4 (8/46) 15.2 (7/46) 17.4 (8/46) 50.0 (23/46)
Vascular invasion of the parametria	26.1 (12/46)

*: median (interquartile range, IQR)

Table 2. Kappa-values and percentage of observed inter-rater agreement (with respective 95% CIs) for each item.

Items	K-value (95% CI)	Agreement (%) (95% CI)
1: Presence of PAS: a) *Present* b) *Not present* c) *Unsure*	0.90 (0.89-1)	92.1 (86.8-94.0)
2. Depth of PAS: *a) Placenta creta* *b) Placenta increta* *c) Placenta percreta*	0.95 (0.89-1)	98.9 (96.8-100)
3. Topography of placental invasion (sagittal plane): *a) Bladder invasion, postero-superior segment (S1)* *b) Bladder invasion, postero-inferior segment+cervix (S2)* *c) Bladder invasion not visible*	0.56 (0.54-0.66)	72.8 (72.7-72.9)
4. Placental invasion of the parametrium (coronal plane): *a) Present* *b) Absent* *c) Doubtful*	0.69 (0.59-0.71)	86.6 (86.5-86.7)
5. Placental invasion of the parametrium (axial plane): *a) Present* *b) Absent* *c) Doubtful*	0.56 (0.33-0.60)	78.6 (78.5-78.7)
6. Newly formed vessels in the parametrial tissue (axial plane): ***a)*** *Present* ***b)*** *Absent*	0.59 (0.45-0.68)	88.0 (88.0-88.1)
7. If present, number of newly formed vessels in the parametrial tissue: ***a)*** *Few* ***b)*** *Many*	0.22 (0.12-0.37)	66.7 (66.6-66.7)

8. Placental location: *a) Anterior* *b) Posterior* *c) Lateral* *d) Fundal*	1 (-)	100 (100-100)
9. Coverage of the IUO by the placenta: *a) Completely covered* *b) Uncovered*	0.95 (0.89-1)	98.9 (96.8-100)
10. Placental imaging appearance: *a) Homogeneous* ***b)*** *Heterogeneous*	0.70 (0.63-0.71)	86.2 (79.4-93.1)
11. Characteristics of the dark intra-placental bands: *a) Thick* *b) Thin* *c) Not visible* *d) Located in the lower uterus* *e) Confluent*	0.59 (0.48-0.65)	74.6 (65.5-83.8)
12. Presence of hemorrhagic placental infarction areas: *a) Yes* *b) No*	0.52 (0.38-0.69)	86.6 (86.5-86.7)
13. Presence of placental venous lakes (lacunae): *a) Yes* *b) No*	0.95 (0.89-1)	98.9 (96.8-100)
14. Number of lacunae (if present): *a) <4* *b) ≥4*	0.80 (0.70-0.86)	90.6 (90.5-90.6)
15. Shape of the lacunae (if present): *a) Regular* *b) Irregular*	0.80 (0.70-0.86)	90.6 (90.5-90.6)

16. Characteristics of the uterine-bladder interface: *a) Myometrium visible* *b) Interrupted interface* *c) Myometrium not infiltrated and visible near the cervix*	0.64 (0.55-0.74)	86.6 (86.5-86.6)
17. Vascularization of the uterine-bladder interface: *a. present; b. absent*	0.48 (0.25-0.79)	75.7 (75.6-75.7)
18. Characteristics of the vascularization (if present) of uterine-bladder interface: *a) With few loci* *b) With multiple loci* *c) Chaotic*	0.64 (0.53-0.69)	83.3 (83.2-83.4)
19. Outward bulging of the placenta: *a) Present* *b) Absent*	0.62 (0.53-0.79)	81.9 (81.8-82.1)
20. Filled bladder: *a) Yes* *b) No*	0.76 (0.68-0.95)	93.5 (93.4-93.5)
21. Presence of artifacts: *a) Yes* *b) No*	0.35 (0.13-0.48)	90.2 (90.1-90.3)

CI = Confidence Interval; ‡ IUO = Internal uterine orifice; Ψ Widening of the lower uterine segment with consequent distortion of the normal inverted pear-shape of the gravid uterus into a hourglass shape.